EXHIBIT C

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DATE: October 4, 2001

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RE: DRAFT U.S. PATENT APPLICATION
METHODS OF TREATING PAIN
OUR REF: CYPR-023/00US

MESSAGE:

Enclosed are draft claims and an outline for the above-referenced patent application.

If you have any questions, please feel free to contact me at the above number, or Ann Pease or (650) 843-5222.

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If you do not receive all of the pages, please call ANIE K. ROCHE at (650) 843-5703 as soon as possible.

3. SUMMARY OF THE INVENTION

This section will describe the various inventions that will be disclosed and claimed, and will include at least the following:

- Method to treat FMS
  - SNRI, which inhibits NE reuptake greater than serotonin reuptake **[[Need to carve out tricyclics. Amitriptyline (1:1.6) and nortriptyline (1:168). Probably do not need to carve out dothiepin as 1:1 ratio. What is the ratio for doxepin and cyclobenzaprine? Any other tricylics that need to be carved out?]]** NARI
  - Sustained release formulation
- Method to treat pain

4. BRIEF DESCRIPTION OF THE FIGURES

5. DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

5.1 Abbreviations

5.2 Definitions

- Dual serotonin norepinephrine reuptake inhibitor – greater inhibition of norepinephrine than serotonin reuptake. Carve out certain tricyclics.
- **Therapeutically** effective amount
- Adjunctively administered:
  - Covers simultaneous administration (with same pill)
  - Simultaneous administration with two separate pills

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- Administration of one, followed by later separate administration of the other

5.3 SNRIs for treating Pain and Fibromyalgia

- Suggestion in art that greater norepinephrine activity increases analgesia
- But, see WO 01/26623
  - Even though noradrenergic pathways play a role in pain transmission, norepinephrine reuptake inhibitors like tricyclics (had to be used in combination with phenylalanine or tyrosine to be effective.) ?
- Present invention is directed to use of SNRIs which inhibit norepinephrine reuptake greater than serotonin reuptake for pain and fibromyalgia.
  - Contrary to the information in the art, administration of SNRIs which inhibit norepinephrine reuptake greater than serotonin reuptake, in the absence of phenylalanine or tyrosine, are effective for treatment of pain and fibromyalgia.

5.4 Sustained release formulations

Include information from the French application.

5.5 Dosages

This section will describe the various doses that can be used.

6. EXAMPLES

This section will describe a prophetic clinical trial on use of milnacipran to treat fibromyalgia.

What is claimed is:

1. A method of treating fibromyalgia and/or associated symptoms of pain in an animal subject, comprising administering to the animal subject, in need thereof, a **therapeutically** effective amount of a dual serotonin norepinephrine reuptake inhibitor compound, wherein said dual serotonin norepinephrine reuptake inhibitor compound is characterized by a greater inhibition of norepinephrine reuptake than serotonin reuptake, and wherein said compound is not administered adjunctively with phenylalanine or tyrosine.

2. The method according to claim 1, wherein the ratio of inhibition of serotonin reuptake to norepinephrine reuptake by the compound is in the range of from about 0.5-1:2-30.

3. The method according to claim 1, wherein the compound is milnacipran ***[[Any other compounds?]]*** → Shuto?

4. The method according to claim 1, wherein fibromyalgia is treated.

5. The method according to claim 1, wherein associated symptoms of pain are treated.

6. The method according to claim 1, wherein the compound is adjunctively administered with ***[[Are there any compounds that could be coadministered with milnacipran, for example to provide synergistic effects.]]*** →

7. The method according to claim 1, wherein the animal subject is a human.

8. The method according to claim 1, wherein the **therapeutically** effective amount is from ***[[Need dosage ranges]]*** 12.5 → 200mg/day

9. The method according to claim 1, wherein the compound is a NMDA receptor antagonist.

10. The method according to claim 1, wherein the compound is formulated in a sustained release dosage formulation.

11. A method of treating pain in an animal subject, comprising administering to the animal subject, in need thereof, a **therapeutically** effective amount of a dual serotonin norepinephrine reuptake inhibitor compound, wherein said dual serotonin norepinephrine reuptake inhibitor compound is characterized by a greater inhibition of norepinephrine reuptake than serotonin reuptake, and wherein said compound is not administered adjunctively with phenylalanine or tyrosine.

12. The method according to claim 11, wherein the ratio of inhibition of serotonin reuptake to norepinephrine reuptake by the compound is in the range of from about 0.5-1:2-30.

13. The method according to claim 11, wherein the compound is milnacipran.

14. The method according to claim 11, wherein the compound is adjunctively administered with ***[[Are there any compounds that could be coadministered with milnacipran, for example to provide synergistic effects.]]***

15. The method according to claim 11, wherein the animal subject is a human.

16. The method according to claim 11, wherein the **therapeutically** effective amount is from ***[[Need dosage ranges]]***

17. The method according to claim 11, wherein the compound is a NMDA receptor antagonist.

18. The method according to claim 11, wherein the compound is formulated in a sustained release dosage formulation.